NON-FINAL ACTION

1. **Claim(s) 1-25** as originally filed 014 AUG 07 is/are pending in this application.

35 USC § 103

2. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

3. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. § 103, the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligations under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of potential 35 U.S.C. § 102(f) or (g) prior art under 35 U.S.C. § 103.

CLAIM REJECTIONS UNDER 35 USC § 103

4. **Claim(s) 1, 3-4, 6-7, 9-13,15-17 and 20-25** is/are rejected under 35 U.S.C. 103(a) as being unpatentable over Todd et al. [Analytical Biochemistry 296 : 179-187(2001)] in view of Ward et al. [Progress in Medicinal Chemistry 38 :309-376 (2001) and Sharpe et al.[US 6,552,066(2003)].

Claim 1 is drawn to a method for identifying a modulator of a biological process which comprises three steps. To begin, a test mixture from a biological process is provided wherein said test mixture is provided under conditions which support

biological activity. Next, a test compound is added to said test mixture. Finally, a difference in the reaction heat rate in the presence of the compound is detected compared to the reaction heat rate in the absence of the compound wherein a difference is indicative that said test compound modulates the activity of the biological process. **Claim 4** is drawn to a method for identifying a modulator of a biological process which is essentially the same method as that recited in Claim 1. **Claim 7** is drawn to a method for identifying a modulator of a biological process which is essentially the same as that recited in Claims 1 and/or 4. **Claim 10** is drawn to a method for identifying a modulator of the activity of a biolmolecule which is essentially the same method(s) as recited in Claims 1, 4 and/or 7. **Claim 20** is drawn to a method for identifying a compound that modulates of the activity of a biomolecule which is essentially the same method(s) as recited in Claims 1, 4, 7 and/or 10. **Claim 23** is drawn to a method for identifying a compound that modulates of the activity of a biomolecule which is essentially the same method(s) as recited in Claims 1, 4, 7, 10 and/or 20.

Todd et al. teach a method for analyzing an enzymatic reaction (i.e. biological process – e.g. protein hydrolysis using trypsin) using micro-isothermal temperature calorimetry (i.e. ITC). Todd et al. do not teach identifying modulators of enzyme activity or the use of controls (i.e. reactions with biological modulators or reactions without biological modulators). However, Ward et al. do teach identifying modulator(s) of a biological process (i.e. an enzymatic reaction), see, at least, for example pp. 360 -370. In addition, Sharpe et al. teach the use of controls in identifying modulators (i.e. inhibitors of Protein Tyrosine Kinase) in a drug discovery assay, see at least, for example Column 10, lines 30 – Column 11, line 20. Therefore, absent an unexpected result it would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to modify the method(s) reasonably suggested by Todd et al. wherein the Todd et al. assay(s) are modified such that modulators of the enzyme reaction are tested as taught by Ward et al. and wherein controls are used to identify modulators of a biological process as taught by Sharpe et al. The ordinary artisan would have been motivated to make the modification recited above in order to utilize ITC in

drug discovery assays as suggested by Todd et al. see the section entitled "Discussion" wherein Todd et al. discuss the benefits of calorimetric assays over conventional methods.

Claim 3 is drawn to an embodiment of the method of Claim 1 wherein the biological process is selected from a defined group which includes protein degradation. **Claim 6** is drawn to an embodiment of the method of Claim 4 wherein the biological process is selected from a defined group which includes protein degradation. **Claim 9** is drawn to an embodiment of the method of Claim 7 wherein the biological process is selected from a defined group which includes protein degradation.

Todd et al . teach these limitations, see at least the abstract.

Claim 11 is drawn to an embodiment of the method of Claim 10 wherein the biomolecule is selected from a defined group which includes a protein. **Claim 12** is drawn to an embodiment of the method of Claim 11 wherein the protein is an enzyme or a polypeptide. **Claim 13** is drawn to an embodiment of the method of Claim 12 wherein the enzyme is from organisms selected from a defined group which includes a prokaryote, a eukaryote or a virus.

Todd et al., Ward et al. and/or Sharpe et al. teach these limitations.

Claim 15 is drawn to an embodiment of the method of Claim 12 wherein the enzyme is from a bacterium.

Todd et al. and/or Ward et al. teach these limitations.

Claim 16 is drawn to an embodiment of the method of Claim 15 wherein the bacterial enzyme analyzed is DNA gyrase or topoisomerase IV.

Ward et al. teach analyzing bacterial DNA gyrase. See at least Ward et al. beginning at about p. 360.

Claim 17 is drawn to an embodiment of the method of Claim 12 wherein the enzyme analyzed is selected from a defined group which includes oxidases/reductases, kinases and ligases.

Todd et al. teach these limitations, see at least the abstract.

Claim 21 is drawn to an embodiment of the method of Claim 20 wherein the biomolecule analyzed is selected from a defined group which includes a protein. **Claim 22** is drawn to an embodiment of the method of Claim 20 wherein the protein analyzed is an enzyme. **Claim 24** is drawn to an embodiment of the method of Claim 23 wherein the biomolecule analyzed is selected from a defined group which includes a protein. **Claim 25** is drawn to an embodiment of the method of Claim 24 wherein the protein analyzed is an enzyme.

Todd et al. teach these limitations, see at least the abstract.

5. Claim(s) 2, 5 and 8 is/are rejected under 35 U.S.C. 103(a) as being unpatentable over Todd et al. [Analytical Biochemistry 296 : 179-187(2001)] in view of Ward et al. [Progress in Medicinal Chemistry 38 :309-376 (2001)] and Sharpe et al. [US 6,552,066(2003)] as applied against Claims 1, 4 and 7 above and further in view of Levy et al. [US 2003/0229065 (2003)] or Price [US 7,018,836 (2006)].

Claim 2 is drawn to an embodiment of Claim 1 wherein biological process is transcription or translation. **Claim 5** is drawn to an embodiment of the method of Claim 4 wherein the biological process is transcription or translation. **Claim 8** is drawn to an embodiment of the method of Claim 7 wherein the biological process is transcription or translation.

Todd et al. in view of Ward et al. and Sharpe et al. reasonably suggest a screening method for identifying a modulator of a biological process which comprises

all of the limitations of Claims 2, 5 and 8 except Todd et al. in view of Ward et al. and Sharpe et al. do not teach identifying modulator(s) of transcription and/or translation. However, as evidenced by Levy et al. and/or Price assays to identify modulators of transcription and/or translation were well known at the time of the invention. Therefore, absent an unexpected result it would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to modify the method(s) reasonably suggested by Todd et al. in view of Ward et al. and Sharpe et al. wherein the biological process of Levy et al. or Price is analyzed rather than the biological processes taught by Todd et al. in view of Ward et al. and Sharpe et al. Please note that substitution of one well known method/reagent with known properties for a second well known method/reagent with well known properties would have been *prima facie* obvious to the ordinary artisan at the time of the invention in the absence of an unexpected result. As regards the motivation to make the substitution recited above, the motivation to combine arises from the expectation that the prior art elements will perform their expected functions to achieve their expected results when combined for their common known purpose. Support for making this obviousness rejection comes from the M.P.E.P. at 2144.07 and 2144.09.

6. **Claim(s) 14** rejected under 35 U.S.C. 103(a) as being unpatentable over Todd et al. [Analytical Biochemistry 296 : 179-187(2001)] in view of Ward et al. [Progress in Medicinal Chemistry 38 :309-376 (2001) and Sharpe et al. [US 6,552,066(2003)] as applied against Claim 12 and further in view of Kmiec et al. [US 5,691,187 (1997)]

Claim 14 is drawn to an embodiment of Claim 12 wherein the enzyme is topoisomerase.

Todd et al. in view of Ward et al. and Sharpe et al. reasonably suggest a screening method for identifying a modulator of a enzyme which enzyme is topoisomerase comprising all of the limitations recited in Claim 14 except Todd et al. in view of Ward et al. and Sharpe et al. do not teach an embodiment wherein the enzyme investigated is a topoisomerase . However, as evidenced by Kmiec et al. topoisomerases, as well as, drug discovery assay which identify modulators of

topoisomerases were well known at the time of the invention. Therefore, absent an unexpected result it would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to modify the method(s) reasonably suggested by Todd et al. in view of Ward et al. and Sharpe et al. wherein the biomolecule analyzed is topoisomerase rather than the enzymes taught by Todd et al. Ward et al. and/or Sharpe et al. Please note that substitution of one well known method/reagent with known properties for a second well known method/reagent with well known properties would have been *prima facie* obvious to the ordinary artisan at the time of the invention in the absence of an unexpected result. As regards the motivation to make the substitution recited above, the motivation to combine arises from the expectation that the prior art elements will perform their expected functions to achieve their expected results when combined for their common known purpose. Support for making this obviousness rejection comes from the M.P.E.P. at 2144.07 and 2144.09.

7. **Claim(s) 18-19** rejected under 35 U.S.C. 103(a) as being unpatentable over Todd et al. [Analytical Biochemistry 296 : 179-187(2001)] in view of Ward et al. [Progress in Medicinal Chemistry 38 :309-376 (2001) and Sharpe et al. [US 6,552,066(2003)] as applied against Claim 12 and further in view of Benson [US 2002/0156585] Black et al. [US 6,310,193 (2001)] or Wei et al. [US 2002/0132331 (2002)].

Claim 18 is drawn to an embodiment of Claim 12 wherein the enzyme is selected from a defined group which includes MurB, MurC and DNA ligase.

Todd et al. in view of Ward et al. and Sharpe et al. reasonably suggest a screening method for identifying a modulator of a enzyme comprising all of the limitations recited in Claim 18 except Todd et al. in view of Ward et al. and Sharpe et al. do not teach an embodiment wherein the enzyme investigated is MurB, MurC and DNA ligase.. However, as evidenced by Benson (see at least paragraph [0016]), Black et al. (see at least Column 12, beginning at about line 29) and Wei et al. (see at least Claim 20) the enzymes recited, as well as, drug discovery assays which identify modulators of the enzymes recited were well known at the time of the invention. Therefore, absent an unexpected result it would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to modify the method(s) reasonably suggested by Todd et al. in view of Ward et al. and Sharpe et al. wherein the biomolecule analyzed is MurB, MurC and DNA ligase rather than the enzymes taught by Todd et al. Ward et al. and/or Sharpe et al. Please note that substitution of one well known method/reagent with known properties for a second well known method/reagent with well known properties would have been *prima facie* obvious to the ordinary artisan at the time of the invention in the absence of an unexpected result. As regards the motivation to make the substitution recited above, the motivation to combine arises from the expectation that the prior art elements will perform their expected functions to achieve their expected results when combined for their common known purpose. Support for making this obviousness rejection comes from the M.P.E.P. at 2144.07 and 2144.09.

Claim 19 is drawn to an embodiment of Claim 12 wherein the enzyme is involved in a process selected from a defined group which includes cell wall biosynthesis and replication.

Please note that both of MurB and MurC of Benson and Black et al. are enzymes involved in cell wall biosynthesis while the DNA ligase of Wei et al is involved in replication.

CONCLUSION

8. **Claim(s) 1-25** is/are rejected and/or objected to for the reason(s) set forth above.

9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ethan Whisenant, Ph.D. whose telephone number is (571) 272-0754. The examiner can normally be reached Monday-Friday from 8:30AM - 5:30PM EST or any time via voice mail. If repeated attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla, can be reached at (571) 272-0735.

The Central Fax number for the USPTO is (571) 273-8300. Please note that the faxing of papers must conform with the Notice to Comply published in the Official Gazette, 1096 OG 30 (November 15, 1989).

/Ethan Whisenant/
Primary Examiner
Art Unit 1634

EXAMINER SEARCH NOTES

11 OCT 08 - ECW

Databases searched: USPATFULL, USPG-PUBS, JAPIO and EUROPATFULL via EAST &

CAplus, Medline and BIOSIS via STN

Reviewed the parent(s), if any, and any search(es) performed therein : see the BIB data sheet

Reviewed, the search(es), if any, performed by prior examiners

Search terms:

Inventor(s) : e.g. Eakin A?/au

Isothermal Titration Calorimetry or ITC

Biological process

Enzyme reaction$

Modulator$

Agonist$ or antagonist$ or inhibitor$

MurB or MurC or Ligase or DNA ligase or

Gyrase or topoisomerase or DNA gyrase or

topoisomerase IV

Transcription or translation